US Army Medical Research and Materiel

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DNA Vaccines Against Poxviruses

This invention is a candidate vaccine that elicits a humoral response which protects against poxviruses. It is a naked DNA vaccine consisting of four vaccinia virus (VACV) gene products, L1R, A27L, B5R and A33R, that has been tested in animals. L1R and A27L encode immunogens located on the intracellular mature virion (IMV) and B5R and A33R encode immunogens located on the extracellular enveloped virion (EEV). When tested in mice, vaccination with a combination of all four genes protected 100% of the mice from a lethal challenge, and weight loss following challenge was similar to the weight loss in mice vaccinated by scarification with live VACV. Vaccination of nonhuman primates with these four plasmids elicited the appropriate humoral response for all four immunogens, including neutralizing antibodies.

Poxviruses include VACV and variola virus, the causative agent of smallpox. Assembly of VACV virions begins with condensation of dense granular material into membrane-wrapped particles called IMV. VACV virions are later released from the cell as EEV which play a role in the long-range spread of the virus. Both the IMV and EEV are infectious forms of poxviruses. The current smallpox vaccine uses live VACV, which has the potential to spread from the vaccination site. Other drawbacks include severe and sometimes lethal adverse reactions, especially in immunocompromised individuals. A poxvirus vaccine is still needed because pathogenic poxviruses and smallpox virus produced by bioterrorists remain a threat. A DNA-based vaccine could conceivably provide effective protection against smallpox, other poxviruses, and engineered vaccinia viruses without the drawbacks of the live vaccine.

If additional VACV immunogens are combined with the current proteins, it may be possible to develop a vaccine that elicits an even more potent and redundant anti-poxvirus immune response. The invention may also help identify targets for the design of a monoclonal antibody-based replacement for human antibody vaccinia immunoglobulin (VIG).

Features and advantages:

- **Elicits humoral responses in nonhuman primates against IMV and EEV vaccinia virus forms**
- **Elicits neutralizing antibodies and protects mice against lethal poxvirus infection**
- **Use of live vaccinia virus is not required**
- **Lethal virus is not disseminated in immunocompromised individuals**
- **Scarring of individuals is avoided**

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